# PMP22 gene

peripheral myelin protein 22

## Normal Function

The *PMP22* gene provides instructions for making a protein called peripheral myelin protein 22 (PMP22). This protein is found in the peripheral nervous system, which connects the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound.

The PMP22 protein is a component of myelin, a protective substance that covers nerves and promotes the efficient transmission of nerve impulses. The protein is produced primarily by specialized cells called Schwann cells that wrap around and insulate nerves. Within Schwann cells, PMP22 plays a crucial role in the development and maintenance of myelin. Studies suggest that the PMP22 protein is particularly important in protecting nerves from physical pressure, helping them restore their structure after compression. Compression can interrupt nerve signaling, leading to the sensation commonly referred to as a limb "falling asleep." The ability of nerves to recover from normal, day-to-day compression, for example when sitting for long periods, keeps the limbs from constantly losing sensation. The *PMP22* gene also plays a role in Schwann cell growth and differentiation (the process by which cells mature to carry out specific functions).

Before it becomes part of myelin, newly produced PMP22 protein is processed and packaged in specialized cell structures called the endoplasmic reticulum and the Golgi apparatus. Completion of these processing and packaging steps is critical for proper myelin function.

## Health Conditions Related to Genetic Changes

### Charcot-Marie-Tooth disease

Mutations in the *PMP22* gene cause several forms of a neurological disorder called Charcot-Marie-Tooth disease.

An extra copy of the *PMP22* gene in each cell is the most common genetic change that causes type 1A Charcot-Marie-Tooth disease. The extra gene leads to an overproduction of PMP22 protein, which prevents the protein from being processed correctly. A reduced amount of functional PMP22 protein impairs the formation of myelin. The unprocessed PMP22 may also disrupt other Schwann cell activities, which leads to instability and loss of myelin (demyelination). Demyelination reduces the ability of the peripheral nerves to activate muscles used for movement or relay information from sensory cells back to the brain. Typically beginning in adolescence,

affected individuals experience weakness and wasting (atrophy) of the muscles of the lower legs and hands and decreased sensitivity to touch, heat, and cold.

Type 1A Charcot-Marie-Tooth disease is also caused by mutations that add, delete, or change the building blocks (amino acids) used to make PMP22 protein. The altered protein is probably processed at a slower rate, and some of the protein is processed abnormally. These disruptions of PMP22 processing impair the normal functions of the Schwann cell, leading to demyelination and producing the signs and symptoms of type 1A Charcot-Marie-Tooth disease.

Hearing loss is experienced by some people with a form of type 1 Charcot-Marie-Tooth disease called type 1E. Type 1E is associated with particular amino acid substitutions and deletions in the *PMP22* gene. The most frequently reported mutation causing hearing loss replaces the amino acid alanine with the amino acid proline at protein position 67 (also written as Ala67Pro).

Some mutations in the *PMP22* gene cause a severe form of Charcot-Marie-Tooth disease sometimes referred to as Dejerine-Sottas disease or type 3 Charcot-Marie-Tooth disease. This form of the disorder usually begins in infancy, causing muscle weakness and atrophy and delayed development of motor skills such as walking.

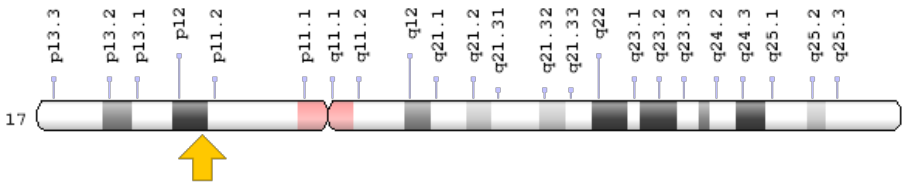
hereditary neuropathy with liability to pressure palsies

Loss of one copy of the *PMP22* gene from each cell is the most common genetic cause of hereditary neuropathy with liability to pressure palsies. This disorder is characterized by recurrent episodes of numbness, tingling, or loss of muscle function, usually triggered by pressure on a nerve in the extremities. Deletion of one copy of the *PMP22* gene reduces the amount of PMP22 protein produced by about half. This disorder is also caused by *PMP22* gene mutations that change single amino acids in the PMP22 protein or that lead to production of an abnormally small protein. These abnormal proteins are rapidly broken down. The consequences of a shortage of PMP22 protein are not clearly understood. Shortage of PMP22 protein may affect the structure of the myelin covering, impairing the transmission of nerve impulses. In addition, the loss of this protein appears to make nerves less able to recover from compression, which also interrupts nerve signaling, causing the signs and symptoms of hereditary neuropathy with liability to pressure palsies.

## Chromosomal Location

Cytogenetic Location: 17p12, which is the short (p) arm of chromosome 17 at position 12

Molecular Location: base pairs 15,229,777 to 15,265,357 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)




Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- GAS-3
- GAS3
- growth arrest-specific 3
- HNPP
- MGC20769
- PMP22_HUMAN
- Sp110

## Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Deficiencies of peripheral nerve myelin https://www.ncbi.nlm.nih.gov/books/NBK28211/#A2798
- Basic Neurochemistry (sixth edition, 1999): Myelin facilitates conduction https://www.ncbi.nlm.nih.gov/books/NBK27954/#A245

GeneReviews

- Charcot-Marie-Tooth Neuropathy Type 1 https://www.ncbi.nlm.nih.gov/books/NBK1205
- Hereditary Neuropathy with Liability to Pressure Palsies https://www.ncbi.nlm.nih.gov/books/NBK1392

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PMP22%5BTIAB%5D%29+OR+%28peripheral+myelin+protein+22%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- HYPERTROPHIC NEUROPATHY OF DEJERINE-SOTTAS
  http://omim.org/entry/145900
- PERIPHERAL MYELIN PROTEIN 22
  http://omim.org/entry/601097

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PMP22.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PMP22%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9118
- Inherited Peripheral Neuropathies Mutation Database
  http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=1
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5376
- UniProt
  http://www.uniprot.org/uniprot/Q01453

## Sources for This Summary


- Al-Thihli K, Rudkin T, Carson N, Poulin C, Melançon S, Der Kaloustian VM. Compound heterozygous deletions of PMP22 causing severe Charcot-Marie-Tooth disease of the Dejerine-Sottas disease phenotype. Am J Med Genet A. 2008 Sep 15;146A(18):2412-6. doi: 10.1002/ajmg.a.32456.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/18698610
- Bai Y, Zhang X, Katona I, Saporta MA, Shy ME, O'Malley HA, Isom LL, Suter U, Li J. Conduction block in PMP22 deficiency. J Neurosci. 2010 Jan 13;30(2):600-8. doi: 10.1523/JNEUROSCI.4264-09.2010.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/20071523
  *Free article on PubMed Central:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3676309/

- Berger P, Young P, Suter U. Molecular cell biology of Charcot-Marie-Tooth disease. Neurogenetics. 2002 Mar;4(1):1-15. Review.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/12030326
- Guo J, Wang L, Zhang Y, Wu J, Arpag S, Hu B, Imhof BA, Tian X, Carter BD, Suter U, Li J. Abnormal junctions and permeability of myelin in PMP22-deficient nerves. Ann Neurol. 2014 Feb; 75(2):255-65. doi: 10.1002/ana.24086. Epub 2014 Feb 20.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/24339129
  *Free article on PubMed Central:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4206215/
- Jetten AM, Suter U. The peripheral myelin protein 22 and epithelial membrane protein family. Prog Nucleic Acid Res Mol Biol. 2000;64:97-129. Review.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/10697408
- Katona I, Wu X, Feely SM, Sottile S, Siskind CE, Miller LJ, Shy ME, Li J. PMP22 expression in dermal nerve myelin from patients with CMT1A. Brain. 2009 Jul;132(Pt 7):1734-40. doi: 10.1093/brain/awp113. Epub 2009 May 15.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/19447823
  *Free article on PubMed Central:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2724915/
- Niedrist D, Joncourt F, Mátyás G, Müller A. Severe phenotype with cis-acting heterozygous PMP22 mutations. Clin Genet. 2009 Mar;75(3):286-9. doi: 10.1111/j.1399-0004.2008.01120.x. Epub 2008 Nov 29.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/19067730
- Niemann A, Berger P, Suter U. Pathomechanisms of mutant proteins in Charcot-Marie-Tooth disease. Neuromolecular Med. 2006;8(1-2):217-42. Review.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/16775378
- Rosso G, Liashkovich I, Gess B, Young P, Kun A, Shahin V. Unravelling crucial biomechanical resilience of myelinated peripheral nerve fibres provided by the Schwann cell basal lamina and PMP22. Sci Rep. 2014 Dec 2;4:7286. doi: 10.1038/srep07286.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/25446378
  *Free article on PubMed Central:* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4250911/
- Rossor AM, Polke JM, Houlden H, Reilly MM. Clinical implications of genetic advances in Charcot-Marie-Tooth disease. Nat Rev Neurol. 2013 Oct;9(10):562-71. doi: 10.1038/nrneurol.2013.179. Epub 2013 Sep 10. Review.
  *Citation on PubMed:* https://www.ncbi.nlm.nih.gov/pubmed/24018473


---


Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/PMP22

Reviewed: July 2016
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services